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EXAMINER	
SNYDER, STUART	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,493	FLEISCHER ET AL.	
	Examiner	Art Unit	
	STUART W. SNYDER	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☒ Claim(s) *1-3,6-11,14,15,19 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/4/2006, 11/7/2006, 11/15/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-13 and 15-20) drawn to a biosensor comprising the following elected species elements—Protein A, bacterium and antibiotics—in the reply filed on 11/5/2008 is acknowledged. The traversal is on the ground(s) that the special technical feature is not anticipated in prior art but rather requires the teaching of two references. This is found to be persuasive and the restriction requirement is **withdrawn**.

Claim Objections

2. Claim 2 is objected to because of the following informality: Claim 2 recites "proteins A, G or G‴". However, each of these protein names (Protein A, Protein G and Protein G′) is a proper noun and as such should be capitalized. Appropriate correction is required.

3. Claim 8 is objected to because of the following informality: Claim 8 recites "…an Ag/AgCl reference.". However, it is clear from the Specification that the word "electrode" should follow the word reference.

Drawings

4. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description:

Figure 1 contains the character “10” apparently in reference to the chip portion of the biosensor device of the Application as evidenced by such label in Figure 4.

Figures 1 and 4 each contain the character “10”, however an exhaustive review of the Specification failed to provide a description of the element of the biosensor corresponding to the character "10".

Figure 5 contains an apparent typographical error in reference to the electrode spacing; certain text recites "Electrode spacing ≤ 10". However, the Specification (see, especially page 5, line 22) indicates that the spacing should be “less that 1 μm” thus making it unclear what the dimension of the electrode spacing is intended by Applicants.

Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1, in lines 6-7, the phrase "a gap between the electrode pair" is vague and indefinite. It is not clear that "a gap between the electrode pair' refers to the gap between the electrode fingers.

6. Claim 1 recites the limitation "from a sample to be analyzed" spanning lines 17 and 18. There is insufficient antecedent basis for this limitation in the claim.

7. In claim 3, in line 4 and also in claim 15, line 3, the phrase "a directed binding" is vague and indefinite. The specification does not define the phrase and it is not clear as to what the phrase "a directed binding" means.

8. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites “the reference electrode represents an Ag/AgCl reference”. It is clear from the specification that the reference electrode may be an Ag/AgCl reference electrode, however no guidance in the Specification is provided to understand the meaning of an electrode that “represents an Ag/AgCl reference". The phrase lacks meaning in the context of the invention. Thus, the meaning of the claim is unclear.

9. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites “the reference electrode is integrated onto the one reference electrode”. It is unclear and nonsensical as to how an entity may be integrated onto itself. Thus, the claim is indefinite because of the ambiguous language of the quoted phrase.

10. Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claims 12 and 13, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and

invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 4-9, and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter, *et al.* (U.S. Patent. No. 6,673,533, Filed Sep. 17, 1997) in view of El Shami *et al.* (U.S. Patent No. 4,778,751, Filed May 12, 1986) and Niwa *et al.* (Analytical Chemistry, 1990, Vol. 62, pp447-452).

The claims are drawn to a biosensor comprising a silicon substrate, at least one interdigital electrode pair (IDE), a counter electrode accommodated on the silicon substrate, a reference electrode, a first layer made of protein at least covering over the IDE structure, a second protein layer applied over the first protein layer further comprising an antibody selective for the predetermined antigen, and a second antigen-specific antibody capable of generating a signal capable of being detected by the IDE if said predetermined antigen is present in the sample applied to the biosensor. Claims 4-9 and 18-20 add the following limitations: Signal is detected by either alternating current of cyclic voltammetry, the biosensor is coupled with a potentiostat, the sample is provided as a fluid *via* a flow system, the IDE and counter-electrodes are made of gold, the reference electrode is an Ag/AgCl electrode, and the reference electrode is integrated on the biosensor.

Wohlstadter *et al.* teaches a biosensor for determining an antigen—an allergen-specific immunoglobulin E (IgE)—using antigen/antibody coupling comprising a silicon substrate (column 13, lines 36-40), at least one interdigital electrode pair structure applied to the silicon substrate (column 40, lines 32-35 and Fig. 19), a counter electrode applied to a silicon substrate (column21, lines 66-67 and column 40, lines 37-40), a reference Ag/AgCI electrode (column 42, lines 40-42), a first coat made from protein covering at least the interdigital electrode structure (column 8, lines 29-33 and column 102, lines 3- 6), a selective second coat made from protein applied over the first coat, which contains a selected captor antibody (column 22, line 23), a third coat applied over the second coat, containing the allergen (column 49, line 34) which is coupleable to the captor antibody, and a sensor signal, which is readable at the interdigital electrode pair structure, wherein an enzymatic release of a redox reactive molecule (column 35, lines 5-9) takes place at the sensor surface via an enzyme-marked detection antibody (column 1, lines 37-38). However, Wohlstadter fails to teach an assay, in which samples of human blood serum in contact with the biosensor couples an allergen-specific IgE to the allergen present on the sensor surface and the electrode pair having a maximum gap of 1.0 µm.

El Shami *et al.* teaches a method of detecting allergen-specific IgE by coupling a sample of human blood serum suspect of containing the allergen-specific IgE to an immobilized allergen on a solid support followed by coupling a labeled anti-IgE antibody to the allergen-specific IgE (column 2, line 67-column 3, line 12).

Niwa *et al.* teaches an interdigitated array (IDA) electrodes having gap ranging from 0.75-10 μm (p448, Table I). The magnitude of the limiting currents at these IDA electrodes is increased by decreasing the gap in the IDA and corresponds to the theoretical value. Furthermore, the collection efficiency is increased by decreasing the electrode size (p448, Table I and Results and Discussion, Collection Efficiencies of IDA's With Different Geometric Parameters, lines 14-19).

With respect to claim 4, Niwa *et al.* teaches detection methods, which include a cyclical voltammetry (p 447, Introduction, lines 5-6).

With respect to claims 5 and 18, Wohlstadter, *et al.* teaches a biosensor coupled to a potentiostat in order to read out the sensor signal (column 10, lines 3-7).

With respect to claims 6, 19, and 20 Wohlstadter, *et al.* teaches a flow system (microfluidic device), which provides sample fluid on the surface of the biosensor (column 18, lines 31-34).

With respect to claim 7, Wohlstadter, *et al.* teaches a biosensor, wherein interdigital electrode structures and counter electrodes are made from gold (column 29, lines 25-28).

With respect to claims 8 and 9, Wohlstadter *et al.* teaches a biosensor, wherein the reference electrode represents an Ag/AgCI reference and the reference electrode is integrated onto the biosensor (column 42, lines 40-42).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the biosensor of Wohlstadter, *et al.* with the

antigen detection method of El Shami, *et al.* in order to detect antigens from various samples, including those derived from human blood. Furthermore, it would also have been obvious to one of ordinary skill in the art at the time of the invention to include in the biosensor of Wohlstadter, *et al.* with the IDA electrode geometric configuration of Niwa, *et al.* in order to increase collection efficiency as taught by Niwa, *et al.*

13. Claims 2, 3, and 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter, *et al.* (U.S. Patent. No. 6,673,533, Filed Sep. 17, 1997) in view of El Shami, *et al.* (U.S. Patent No. 4,778,751, May 12, 1986) and Niwa, *et al.* (Analytical Chemistry, 1990, Vol. 62, pp447-452) as applied to claim 1 above, and further in view of Pettit, *et al.* (U.S. Patent No. 6,548,644, Filed Mar. 10, 1997).

The limitations of claim 1 are summarized above (see section 12). Claims 2, 3, 11-17 add the following limitations: The first protein layer consists of one of Protein A, Protein G or Protein G′; the first and second protein layers are specific binding partners; the antigen is peptidyl, microorganism, or an organic compound; the signal is detected using alternating current or cyclic voltammetry; and claim 14 claims a method of use of the biosensor and incorporates limitations of certain of the dependent claims rejected herein.

Wohlstadter, *et al.* in view of El Shami, *et al.* and Niwa, *et al.* teaches a biosensor as discussed above. However, Wohlstadter, *et al.* in view of El Shami, *et al.* and Niwa *et al.* fails to teach the biosensor, wherein the first protein coat is made

from at least one proteins selected from Protein A, Protein G, Protein G' and Protein L.

Pettit teaches the use of a substrate immobilized with Protein A or Protein G prior to antibody immobilization (column 6, lines 53-56). Antibodies immobilized in this fashion have a spatial orientation, which provides for their maximal binding with the protein selected for conjugation.

With respect to claims 12 and 15, Niwa, *et al.* teaches detection methods, which include a cyclical voltammetry (p 447, Introduction, lines 5-6).

With respect to claims 13 and 16, Wohlstadter, *et al.* teaches a biosensor coupled to a potentiostat in order to read out the sensor signal (column 10, lines 3-7).

With respect to claims 14 and 17, Wohlstadter, *et al.* teaches a flow system (microfluidic device), which provides serum sample fluid on the surface of the biosensor (column 18, lines 31-34).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the biosensor of Wohlstadter *et al.* in view of El Shami, *et al.* and Niwa, *et al.* with the use of a substrate immobilized with Protein A or Protein G as taught by Pettit, *et al.* in order to achieve maximal binding of the immobilized antibodies with their antigens.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to STUART W. SNYDER whose telephone number is (571)272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/
Primary Examiner, Art Unit 1648

Stuart W Snyder
Examiner
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sws